

Application No.: 09/067,638

Remarks/Arguments

This Amendment is being filed in response to the Office action dated October 12, 2006. Amendments to the claims have been made. Support for the amendments to the independent Claims 83, 85-87 can be found, for example, throughout the specification and as detailed in the following remarks.

Support for the amendments to claim 87 is found specifically at page 16, lines 8-16; Figure 3; page 14, lines 16-19 page 15, lines 3-9 and lines 13-16.

Support for the amendments to claim 83 is found specifically at page 16, lines 8-16; Figure 3, as well as page 25, line 2 and page 26, lines 3-5.

Support for the amendment to claims 85-87 is found at page 25, line 2 and page 26, lines 3-5 (for targeting a functional region); at page 25, lines 27-29 (for targeting accessible sites; See also Example 13 for the result of targeting accessible sites); and at page 25, line 35 to page 26, line 9 (for uniform distribution; See also Example 2 for the result of a uniform distribution).

No new matter is added by these amendments. Each ground of rejection is discussed in detail below under a separate heading.

Rejection under 35 USC § 112, ¶ 1 (New Matter)

Claim 87 has been rejected as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time of the application was filed, had possession of the claimed invention.

The Examiner alleges that the limitation in claim 87, "wherein said computer system searches at least one database for alternative transcripts for said selected nucleic acid;" is new matter. Applicants respectfully disagree.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116.

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While it is understood that newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure, there is no *in haec verba* requirement. MPEP 2163.

As noted by the Examiner, the specification provides adequate support for searching for additional target information (See Figure 3 and page 16, lines 8-16) and that multiple transcripts such as those resulting from alternative splicing (alternative transcripts) may be unique targets for use in the invention. Office Action page 3. Examiner asserts, however, that the specification does not disclose the idea that multiple transcripts (i.e., the alternative transcripts) are those found in a database or that searching at least one database for any kind of transcript, specifically the alternative transcripts, is disclosed.

Applicants note that at the time of filing, it was common knowledge in the art that alternative transcript sequence information could be identified by searching the publicly available sequence databases. It is also Applicants' position that, on reading the instant disclosure, a person of skill in the art would appreciate that there was adequate disclosure for the limitation.

Specifically, at page 14, lines 16-19 it is disclosed that "Any nucleotide sequence, no matter how determined, of any nucleic acid, isolated or prepared in any fashion, may be used as a target nucleic acid in the process of the invention." (emphasis added). At page 15, lines 3-9 it is disclosed that sequence information is "**often deposited in different databases**" and that the process of the invention takes advantage of "fragment assembly algorithms to **search available databases for related sequence information.**" (emphasis added). In addition, at lines 13-16, it is disclosed that where genes undergo alternative splicing, each transcript is a unique target. Obviously the products of alternative splicing are alternative transcripts, and since the synthesis of these transcripts is directed from a single gene, they have, by definition, related sequence information. Taken together, these disclosures make it clear that the invention embraces, and the specification adequately discloses, and the Applicants were in possession of, the limitation "wherein said computer system searches at least one database for alternative transcripts for said selected nucleic acid" to one of skill in the art. The fact that the limitation is not present in the disclosure, *ipsis verbis*, is not the threshold Applicants

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must meet. Consequently, it is Applicants' belief that the disclosure adequately supports the limitation and withdrawal of the rejection is requested.

Rejection under 35 USC § 112, ¶ 2

For various reasons, claims 83-87 have been rejected as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the Office Action, the Examiner points to specific terms and phrases in the claims which are allegedly indefinite. Each term or phrase is addressed here.

The phrase: "based on"

According to the Examiner, in claims 83, 85, 86 and 87, the phrase "based on" is unclear. The claims have been amended to clarify the subset generation criteria. Support for the amendment to claim 83 is found at page 25, line 2 and page 26, lines 3-5.

Support for the amendment to claims 85-87 is found at page 25, line 2 and page 26, lines 3-5 (for targeting a functional region); at page 25, lines 27-29 (for targeting accessible sites; See also Example 13 for the result of targeting accessible sites); and at page 25, line 35 to page 26, line 9 (for uniform distribution; See also Example 2 for the result of a uniform distribution).

The term "targeting"

According to the Examiner, in claims 83, 85, 86 and 87 the term "targeting" renders the claim indefinite. The claims have been amended to clarify step (iii). This step now recites the generation of a subset of said set of virtual oligonucleotides, said subset being the result of a decision to: a) target a functional region of said selected nucleic acid, b) target an accessible site on said selected nucleic acid, and/or c) uniformly distribute oligonucleotide compounds across said selected nucleic acid. The phrase "to target" is intended to carry the customary meaning in the art of antisense technology and in light of the disclosure. Hence, in step (iii), in order to generate a subset of virtual oligonucleotides, decisions are made regarding whether to target functional regions, and/or accessible sites of a selected nucleic acid. The process of "targeting" a particular

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region or site simply means that process of selecting a region or site, with the particular selection being informed by those considerations disclosed in the specification. Therefore the generation of the subset in step (iii) is the result of evaluating the considerations relevant to functional regions and accessible sites, such as for example selecting a functional region (e.g., the transcriptional start site) as discussed at page 25, lines 3-20, and eliminating those members of the set of virtual oligonucleotides which fail to satisfy the selection criteria (e.g., are not the reverse complement of the selected functional region). Applicants believe the rejection to now be moot and respectfully requests withdrawal of the rejection based on the amendments to the claims.

The phrase "target accessibility" and the term "target"

According to the Examiner, in claims 85, 86 and 87 the phrase "target accessibility" and the term "target" render the claims indefinite. Applicants respectfully disagree. As stated above, the claims have been amended to clarify step (iii). It is Applicants' belief that these amendments render the claims definite and overcome the rejection.

The phrase "uniform distribution of oligonucleotide compounds across said selected nucleic acid"

According to the Examiner, in claims 85-87, the phrase "uniform distribution of oligonucleotide compounds across said selected nucleic acid" renders the claims indefinite. Applicants respectfully disagree. The claims have been amended to clarify step (iii) as discussed above. Support for the amendment can be found at page 25, line 35 to page 26, line 9 and in Example 2 which discusses the manual selection of oligonucleotide sequences throughout the target sequence based on the criteria of uniform distribution. Also, original Figure 22 at step 2528 discloses the manual selection of a group of oligonucleotides that provide a random and uniform distribution along the entire gene target sequence. The outcome of such a selection, the 84 oligonucleotides chosen for the gene target CD40, is shown in Table 7.

It would be apparent to one of skill in the art that at step (iii) a larger set of virtual oligonucleotides which have a particular length (required by step (i)) is being selectively

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reduced to a subset of virtual oligonucleotides based on specific selection criteria. It is a basic tenet of the invention and of antisense technology that these oligonucleotides each have a sequence which is the reverse complement of, (i.e., is antisense to) some region or site on the selected nucleic acid. In deciding whether these oligonucleotides will be uniformly distributed across said selected nucleic acid, it is unnecessary to invoke a consideration of *in silico* "hybridization". Subpart (c) of step (iii) only requires that one decide whether or not to choose those members in the set in a fashion which satisfies the distribution criteria disclosed in the specification. If one were still unclear regarding this limitation, the specification provides a working example of such a uniform distribution for the CD40 gene as well as the goal for selecting a uniform distribution—that being, "to provide complete coverage throughout the complete target nucleic acid or the selected functional region." Page 26, lines 6-9. In light of the disclosure and in view of the amendments, Applicants believe the claims are definite and that the rejection has been overcome. Withdrawal of the rejection is respectfully requested.

The phrases "said set of real oligonucleotides" and "said real oligonucleotides"

According to the Examiner, in claims 83, 85- 87 the phrases "said set of real oligonucleotides" and "said real oligonucleotides" render the claims indefinite. The claims have been amended to refer to the synthesized oligonucleotides as "synthesized" instead of "real." Support for these amendments is found throughout the specification and particularly beginning at page 39, Section 13: Description of Automated Oligonucleotide Synthesis.

In light of the disclosure and in view of the amendments, Applicants believe the claims are definite and that the rejection has been overcome. Withdrawal of the rejection is respectfully requested.

The phrase "second apparatus" and relationship to other steps.

According to the Examiner, claim 85 is indefinite because, of the techniques listed for analysis, none are actually apparatuses and further because the step involving the second apparatus recites no relationship to other steps. It is believed that the amendments to Claim 85 overcome the rejection and withdrawal of the rejection is respectfully requested.

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The phrase "modulating said selected nucleic acid"

According to the Examiner, claim 86 contains the redundant phrase, "modulating said selected nucleic acid." Applicants have amended the claim to remove the superfluous phrase and thank the Examiner for so noting it. No new matter was added by this amendment.

The phrase "said property"

According to the Examiner, in claim 86 contains the phrase "said property" which lacks antecedent basis. As stated above, the superfluous phrase has been removed and in so doing renders this rejection moot. Withdrawal of the rejection is respectfully requested.

Dependence of claim 84 on rejected claim

Finally, claim 84 is rejected as indefinite as it depends from claim 83, which has been rejected for being indefinite. Applicant believes that the amendments made to claim 83 render this rejection moot.

Conclusion

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 251-3509.

Respectfully submitted,

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Dated: 2/9/07